

were submitted and entered in the “parent” application (now U.S. Patent No. 5,906,978) of the present continuation application.

The amendments to page 31, line 17 and to page 33, line 13 are supported by Fig. 1, which shows that the transferrin iron binding capacity is 234 µg/dl rather than 225 µg/dl.

The amendments to page 23, line 4; page 25, line 2; and page 31, line 3 all correct typographical errors in the specification. The amendments to page 18, line 7; page 28, line 3; and page 32, line 9, are for purposes of clarification.

#### Remarks Regarding Rejection Under 35 U.S.C. §112, Second Paragraph

In the outstanding Office Action claims 24-39 are rejected under 35 U.S.C. §112, second paragraph. The Examiner states in the Action that “the use of the term ‘such’ in independent claims renders the claims indefinite.”

In order to moot this issue and expedite the allowance of the present case, Applicant requests entry of the above amendments to claims 24 and 32. Said claims, as amended, do not include the word “such.” It is submitted, however, that the original form of these claims satisfied the definiteness requirement of 35 U.S.C. §112, second paragraph, and that the Examiner has improperly created and applied a *per se* rule (quoted above) without citing any authority for the same. Nevertheless, in view of the above amendments, Applicant requests withdrawal of the rejection of claims 24-39 under 35 U.S.C. §112, second paragraph.

#### Remarks Regarding Rejection Under 35 U.S.C. §103(a)

In the outstanding Office Action, claims 24-45 are rejected under 35 U.S.C. §103(a) as being unpatentable over the combined teachings of Jensen and Bastani et al.

In traversal of this rejection, Applicant submits that the Examiner has not established a *prima facie* case of §103(a) obviousness because there is no teaching, suggestion or motivation to modify the references or to combine their teachings in the manner that the Examiner has stated is obvious. In addition, Applicant notes that the Bastani et al. reference is dated November 1996, and that the present application claims priority to a provisional patent application filed on August 14, 1996. Without admitting that this reference is prior art, Applicant submits that its status as prior art is not material because claims 24-45 are not obvious in view of the combination asserted by the Examiner.

To establish a *prima facie* case of obviousness, the Examiner must identify in the prior art some teaching, suggestion or motivation to combine or modify the cited references. "Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art." (citations omitted). Manual of Patent Examining Procedure ("MPEP") §2143.01. "When prior art references require selective combination . . . to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself." Uniroyal v. Rudkin-Wiley, 5 U.S.P.Q. 2d 1434, 1438 (Fed. Cir. 1988) (quoting Interconnect Planning Corp. v. Feil, 227 U.S.P.Q. 543, 551 (Fed. Cir. 1985)). Some teaching in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination. Lindemann Maschinenfabrik GmbH v. American Hoist and Derrick Co., 221 U.S.P.Q. 481, 488 (Fed. Cir. 1984).

The only suggestion to provide and use a composition as recited in the pending claims is provided by the present application. It is respectfully submitted that the Examiner has identified no such teaching, suggestion or motivation in the prior art, and indeed, that the prior art teaches away from the present invention. The Examiner appears to be making the assertion that the claimed invention would be obvious because it is well known that various patients have electrolyte requirements and that various patients have iron requirements. In this regard, it is stated in the Action that, "Given the well known electrolyte requirements of various patients suffering from a variety of ailments, one having ordinary skill in the art would have been motivated to utilize the iron complexes of the instant invention with the expectation that the patient would receive iron and other electrolytes/nutrients." (Office Action, page 2).

Applicant submits, however, that neither the above-quoted statement in the Action nor the cited references provide any teaching, suggestion or motivation to make or use the present invention. Indeed, the specification of the present application describes at great length the problems in the prior art associated with the delivery of iron to patients, which problems are addressed by the invention in a unique manner.

The importance of electrolytes in a dialysate composition is well known. The electrolytes in the dialysate function to maintain electrolyte stability in blood during dialysis. Prior to the present invention, however, there was no teaching, suggestion or motivation to incorporate inventive iron complexes into a dialysate to achieve iron delivery during dialysis and, as discussed more fully below, the prior art teaches away from such incorporation. It is further submitted that Applicant is not aware of any teaching, suggestion or motivation in the prior art to incorporate inventive iron

complexes into any other aqueous composition having the recited concentrations of electrolytes for any other use.

The Jensen patent is cited in the Action as disclosing “metal proteinates such as Iron (sic) proteinates for enhancing uptake of essential minerals.” Jensen discloses that various metals can be assimilated into a living organism if they are made available to the organism “in the form of chelated coordination complexes with amino acids and other hydrolysis products of proteins in a buffered state at a relatively constant pH.” (col.1, lines 31-38). As is readily understood by a person skilled in the art, assimilation in an animal involves the absorption of nutrients and other substances through the epithelial cells of the digestive tract. As stated in Jensen, “For purposes of this application, it is irrelevant at which portion along the digestive tract the assimilation of the metal proteinate occurs.” (col. 1, lines 56-68). While various electrolytes are present in certain compositions described in Jensen, the concentrations of the electrolytes are much lower than the concentrations recited in the pending claims, and there is no suggestion that higher concentrations of electrolytes would ever be desired.

Jensen also notes in passing that, as an alternative to oral ingestion or administration by means of a stomach tube, a metal proteinate may be given by injection intramuscularly, intravenously or subcutaneously. There is no suggestion in Jensen, however, that it would be desirable in connection with any iron delivery protocol to combine a metal proteinate with a solution having an electrolyte concentration of from about 223 mEq/L to about 12,940 mEq/L, as recited in each of pending claims 24-45, as amended.

Although it is not specifically stated in the Office Action, the Examiner appears to be basing this rejection upon a conclusion that it would be obvious to place the metal

proteinate of Jensen into the dialysis solution of Bastani et al. Bastani et al. describe the treatment of a patient by mixing an iron-dextran complex with 1.5% Dianeal PD solution, a 1.5% dextrose solution. The resulting composition was instilled into the patient's peritoneal cavity and allowed to dwell overnight before being drained.

A person of ordinary skill in the art, however, would not be motivated to combine the references in the manner suggested by the Examiner. On the contrary, the prior art actually teaches away from including an iron complex in accordance with the present invention in a dialysate composition because the combination of an inventive iron complex and a dialysate has historically been considered extremely dangerous. As stated at page 7 of the present application, "it is widely believed that soluble iron complexes are unacceptable iron delivery agents, this belief being based upon a fear of the toxicity of free iron in blood." (Specification, page 7, lines 5-8).

Because of this widespread belief, the prior art would motivate a skilled artisan to ensure that an inventive iron complex is not administered to a patient in such a way that the complex would be transported to the patient's blood, such as, for example, via dialysis. Indeed, the protocol used by Bastani et al. is consistent with this prior art belief. Bastani et al. incorporated iron-dextran into a dialysate. Iron-dextran is a very large macromolecule that releases iron only by the action of metabolism, and is not an "iron complex" as that term is defined in the present application. Its use by Bastani et al. thereby avoided the use of an iron complex, as defined in the present application, in keeping with the prior art belief that such iron complexes are dangerous. (See specification, page 4, lines 12-17). Thus, the prior art teaches away from incorporating an iron complex in accordance with the present

invention into the dialysate of Bastani et al. or any other dialysate. For this and other reasons, the prior art teaches away from the present invention.

In addition, even the inclusion of the iron proteinate set forth in Jensen into the dialysate of Bastani et al. does not result in a composition as set forth in pending claims 24-45, as amended. A limitation recited in the pending claims is that the aqueous composition comprises "a plurality of electrolytes dissolved in the water, the electrolytes having a concentration in the water of from about 223 mEq/L to about 12,940 mEq/L." Neither of the cited references, nor a combination of the references, teaches or suggests an aqueous composition comprising the above-recited concentration of electrolytes.

In view of the above, Applicant submits that there is no teaching, suggestion or motivation in the prior art to combine an iron complex in accordance with the invention with water and "a plurality of electrolytes dissolved in the water, the electrolytes having a concentration in the water of from about 223 mEq/L to about 12,940 mEq/L" as recited in the pending claims (as amended). As shown in the specification and discussed above, the prior art teaches away from introducing iron to a patient in this manner.

Without the benefit of hindsight gained from viewing the present application, one having ordinary skill in the art at the time of the invention would not have selected an ingredient from the Jensen reference, and placed the ingredient in a dialysate solution or any other electrolyte solution as recited in the claims. Indeed, there is no suggestion in the prior art that this be done, even in view of the difficulties that had been encountered in the prior art of delivering iron to iron-deficient patients (See pages 2-6 of the specification).

The Examiner has simply used Applicant's claims as a recipe to pick and choose isolated facets out of diverse art. "The result is that the claims were used as a frame, and

individual, naked parts of separate prior art references were employed as a mosaic to recreate a facsimile of the claimed invention.” W.L. Gore & Assoc. Inc. v. Garlock, Inc., 220 U.S.P.Q. 303, 312 (Fed. Cir. 1983). At no point has the Examiner explained why that mosaic would have been obvious to one skilled in the art at the time of the invention, or what there was in the prior art that would have suggested this combination. “To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.” Id. at 312-13. Because there is no suggestion of combination to be found within the cited references, Applicant respectfully submits that claims 24-45 are allowable over the references of record and requests that the rejection under 35 U.S.C. §103 be withdrawn.

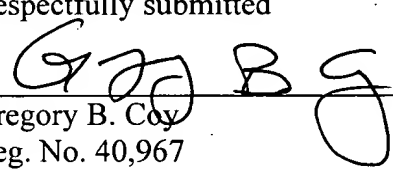
In addition to the above, there are further reasons that the §103 rejection should be withdrawn. For example, to establish a *prima facie* case of obviousness, the prior art reference (or references, when combined) must teach or suggest all the claim limitations (See MPEP §2142). In this regard, Applicant disagrees with the statement in the Action that “every element of the invention has been collectively taught by the combined teachings of the references.” As stated above, a limitation recited in the pending claims is that the aqueous composition comprises “a plurality of electrolytes dissolved in the water, the electrolytes having a concentration in the water of from about 223 mEq/L to about 12,940 mEq/L.” Neither of the cited references, nor a combination of the references, teaches or suggests an aqueous composition comprising the above-recited concentration of electrolytes. As mentioned above, some electrolytes are present in certain solutions described in Jensen; however, the concentrations of the electrolytes are much lower than the concentrations

recited in the pending claims. Furthermore, Applicant submits that there is no mention in Bastani et al. of any electrolytes in the composition set forth therein. Therefore, all claim limitations are not taught or suggested in the cited references, and the rejection under §103 is improper for this reason as well.

For the reasons stated herein, Applicant submits that the present application, as amended and containing claims 24-45, is in condition for allowance. Action to that end is therefore respectfully solicited.

Respectfully submitted

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